REMARKS

A. THE AMENDMENTS TO THE CLAIMS

Claims 1-19, 26-36, and 45-61 are pending. Claims 26-36 and 45-61 are withdrawn from consideration, and claims 1-19 are currently under examination.

Claims 1, 12, and 14 have been amended to clarify that the amino acid sequences of SEQ ID NOs: 6 and 3 are phosphorylated at the threonine residue equivalent to the residue 559 of SEQ ID NO: 5 (i.e., the threonine at position 26 of SEQ ID NO: 6 and the threonine at position 11 of SEQ ID NO: 3). Support for the amendment can be found at page 15, lines 21-24 of the application-as-filed. Claim 12 has been amended to delete reference to "a mutein, functional derivative, active fraction, circularly permutated derivative or salt thereof" and to "portions." No new matter has been added by way of the amendments.

B. THE OFFICE ACTION

The Office rejected claim 12 under 35 U.S.C. § 112, first paragraph, for assertedly lacking enablement commensurate in scope to the claim. The Office also rejected claim 12 under 35 U.S.C. § 112, first paragraph, for assertedly lacking written description. The Office maintained the rejection of claims 1-4, 6-10, 12, 14-16, and 19 under 35 U.S.C. § 102(e) for assertedly being anticipated by U.S. Patent No. 6,822,138 ("Schreiber"). Finally, the rejection of claims 1-10, 12, and 14-19 under 35 U.S.C. § 103(a) for assertedly being obvious over Schreiber in view of Lin et al., *Mol. Cell Biol, 18*(10), 5899-5907 (1998) ("Lin"); Campbell, *Monoclonal Antibody Technology*, Chapter 1, pp. 1-32 (1984) ("Campbell"); Green, *JIM*, 231, 11-23 (1999) ("Green"); and Owens et al., *JIM*, 168, 149-165 (1994) ("Owens") was maintained.

C. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (ENABLEMENT), SHOULD BE WITHDRAWN.

Claim 12 was rejected under Section 112, first paragraph, for assertedly lacking enablement commensurate in scope to the claim. Reconsideration of the rejection is respectfully requested in view of the amendments to the claims and the reasons set forth below.

The Office rejected claim 12 because the specification assertedly does not enable the making or using of an antibody that binds to any mutein, functional derivative, active fraction, circularly permutated derivative, salt, or a portion of NIK. In particular, the Office asserted that one of ordinary skill would not have been able to use the antibody that binds SEQ ID NOs: 5, 6, or 3 to detect all NIK variants or a NIK fragment, mutein, functional derivative, active fraction, circularly permutated derivative, or salts thereof. According to the Office, even slight alterations in target protein structure may abrogate antibody binding and, therefore, an antibody that binds SEQ ID NOs: 5, 6, or 3 will not bind all variants of the peptides.

In an effort to advance prosecution of the instant application, claim 12 has been amended to delete the phrases "or a mutein, functional derivative, active fraction, circularly permutated derivative, or salt thereof" and "or a portion of amino acid sequence." The Office acknowledged that the specification fully enables the anti-NIK antibodies or fragments thereof that bind the amino acid sequence set forth in SEQ ID NOs: 5, 6, and 3. Office Action, p. 3. Thus, the rejection of claim 12 under 35 U.S.C. § 112, first paragraph, has been rendered moot and should be withdrawn.

Applicant continues to disagree with the Office's position, notwithstanding the dispositive amendment to claim 12 made herein and noted above. In support of the rejection, the Office misconstrues claim 12 as drawn to an antibody binding to SEQ ID NOs: 5, 6, or 3 and binding to all variant forms of NIK. Prior to the instant amendment, however, claim 12 was drawn to an antibody binding NIK or any one of the claim-recited variants of NIK, provided that the NIK or variant thereof had a phosphorylated threonine at position 559 of SEQ ID NO: 5 (or equivalent threonine in SEQ ID NOs: 6 and 3). In addition, the Office asserted that a complete or partial structure of an antibody binding all species of NIK recited in the claim was not provided. The statement appears to be based on a misunderstanding of the claim 12 subject matter. The application-as-filed did provide at least a partial structure of the claim-recited antibody in disclosing structures to which the antibody binds, as presented in any of SEQ ID NOs: 5, 6, or 3. Finally, the Office focused on whether an actual reduction to practice of an antibody binding to a NIK variant has been achieved. The focus on an actual reduction to practice is misplaced, as there is no requirement for such a reduction

under § 112, first paragraph. Claim 12, prior to and after entry of the present amendment, is enabled throughout its full scope and, accordingly, the rejection of claim 12 under § 112, first paragraph for lack of enablement commensurate in scope to the claim should be withdrawn.

D. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION), SHOULD BE WITHDRAWN.

Claim 12 was rejected under Section 112, first paragraph, for assertedly lacking written description. Reconsideration of the rejection is respectfully requested in view of the amendments to the claims and the reasons set forth below.

The Office asserted that the specification "does not appear to provide an adequate written description for the all the muteins, functional derivatives, active fractions, circularly permutated derivatives, salts of NIK as targets of the claimed antibodies because there is lack of sufficient written description to support the recited genus of the antibody targets." Office Action, p. 6.

Claim 12 has been amended solely in an effort to advance prosecution of the instant application to delete the phrases "or a mutein, functional derivative, active fraction, circularly permutated derivative, or salt thereof" and "or a portion of amino acid sequence." The Office acknowledged that the specification written description for the anti-NIK antibodies or fragments thereof that bind the amino acid sequence set forth in SEQ ID NOs: 3, 5, and 6. Office Action, p. 7 ("[o]ther than the antibody binding to the SEQ ID NO: 3, 5, and 6, there does not appear to be an actual reduction to practice. . . ."; emphasis added). Although there is no requirement to disclose an actual reduction to practice of any claimed subject matter in a patent application (to provide written description or for any other reason), the Office's implied recognition of the now-claimed subject matter as actually reduced to practice, and more importantly, as supported by a written description, is acknowledged. Thus, the rejection of claim 12 under 35 U.S.C. § 112, first paragraph, has been rendered moot and should be withdrawn.

Beyond the dispositive amendment to claim 12 made herein, Applicant continues to disagree with the Office's position. As explained above, the Office misconstrued claim 12 as drawn to an antibody binding to SEQ ID NOs: 5, 6, or 3 and

binding to all variant forms of NIK. Prior to the instant amendment, however, claim 12 was drawn to an antibody binding NIK or any one of the claim-recited variants of NIK, provided that the NIK or variant thereof had a phosphorylated threonine at position 559 of SEQ ID NO: 5 (or equivalent threonine in SEQ ID NOs: 6 and 3). In addition, the Office asserted that a complete or partial structure of an antibody binding all species of NIK recited in the claim was not provided. The statement is based on a misunderstanding of the claim 12 subject matter. The application-as-filed did provide at least a partial structure of the claim-recited antibody in disclosing structures to which the antibody binds, as presented in any of SEQ ID NOs: 5, 6, or 3. Finally, the Office focused on whether an actual reduction to practice of an antibody binding to a NIK variant has been achieved. The focus on an actual reduction to practice is misplaced as there is no requirement for such a reduction under § 112, first paragraph. A sufficient written description was provided for claim 12, prior to and after entry of the present amendment and, accordingly, the rejection of claim 12 under § 112, first paragraph for lack of written description should be withdrawn.

E. THE REJECTION UNDER 35 U.S.C. § 102(e) SHOULD BE WITHDRAWN.

Claims 1-4, 6-10, 12, 14-16, and 19 were rejected under 35 U.S.C. § 102(e) for assertedly being anticipated by Schreiber. The rejection is respectfully traversed for the reasons set forth below.

To anticipate the pending claims, Schreiber must teach each and every element of the rejected claims. See, e.g., *Verdegaal Bros. v. Union Oil Co. of CA*, 814 F.2d 628, 631 (Fed. Cir. 1987). Claims 1-4, 6-10, 12, 14-16, and 19 are directed to a polyclonal, monoclonal, chimeric, humanized, human or anti-anti-idiotype antibody or fragment thereof (or a pharmaceutical composition comprising the antibody or fragment thereof) capable of specifically binding an amino acid sequence set forth in SEQ ID NOs: 5, 6, or 3 comprising a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5, position 26 of SEQ ID NO: 6, or position 11 of SEQ ID NO: 3. Schreiber apparently discloses a genus of antibodies that bind NIK, but does not teach each and every feature of the claim-recited antibody or antibody fragment that specifically binds NIK protein comprising phosphorylated T559, as recited in the pending claims. Disclosure of a genus does not anticipate a claimed species. *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1367 (Fed.

Cir. 2004) (explaining that "[a] prior art reference that discloses a genus still does not inherently disclose all species within that broad category"). Indeed, the reference does not teach or suggest the specific portion of NIK to which the claimed antibody binds, nor does the reference teach a subset of antibodies that specifically binds a phosphorylated NIK.

The Office improperly ignored the feature of the claim wherein the antibody is capable of "specifically binding" SEQ ID NO: 5, 6, or 3, wherein the amino acid sequence comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5. Antibodies that "specifically bind" are described in the specification as those "that can bind to NIK phosphorylated at T559, but in contrast, they have low binding capacity, or do not bind [at] all to non-phosphorylated NIK." See application, p. 17, lines 14-16. Moreover, Examples 2 and 3 and Figures 4 and 5 demonstrate that the claimed antibodies recognize only the phosphorylated version of NIK. Antibodies that specifically bound the phosphorylated version of the peptide were elicited when the NIK activation loop fragment contained phosphorylated T559 in the penultimate position (i.e., SEQ ID NO: 3). As demonstrated in Figure 4, antibodies raised against SEQ ID NO: 3 phosphorylated at the threonine at position 11 specifically bound NIK phosphorylated at T559 (i.e., the antibodies did not bind to non-phosphorylated NIK). Despite the Office's assertion, Schreiber does not disclose, expressly or inherently, an antibody capable of "specifically binding" phosphorylated NIK, as that term is defined in the specification. Thus, the Office has failed to present a *prima facie* case of anticipation, and the rejection of claims 1-4, 6-10, 12, 14-16 and 19 under 35 U.S.C. § 102(e) over Schreiber should be withdrawn.

Despite the failure of Schreiber to teach each and every element of any of the pending claims, the Office asserted that Applicants must prove that the described genus of polyclonal antibodies would not bind to the recited NIK fragments, suggesting that the disclosed genus of antibodies inherently meets the limitations of the pending claims. To rely on a theory of inherency, however, the Office must provide "a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Interf. 1990). "The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 169 F.3d 743, 745 (Fed.

Cir. 1999) (citations omitted). The Office failed to present evidence or reasoning showing that any prior art antibodies would necessarily bind to portions of NIK containing phosphorylated T559 as recited in the claims and, therefore, has not met the Office's burden. Without such evidence or reasoning, the Office cannot require an applicant to prove that the prior art does not possess the claimed characteristic. M.P.E.P. § 2112(IV); See also *Ex parte Jurg Zimmerman* 2003 WL 25277881, *4 (Bd. Pat. App. & Interf. 2003), quoting *Ex parte Skinner*, 2 U.S.P.Q.2d 1788 (Bd. Pat. App. & Interf. 1986).

Accordingly, Applicants have shown that features of the claimed antibodies are not necessarily found in the genus of anti-NIK antibodies of Schreiber. The reference fails to explicitly or inherently disclose the particular anti-NIK antibodies of the pending claims. Therefore, the rejection of claims 1-4, 6-10, 12, 14-16, and 19 under 35 U.S.C. § 102(e) over Schreiber has been overcome and should be withdrawn.

F. THE REJECTION UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN.

The Office rejected claims 1-10, 12, and 14-19 under Section 103(a) for assertedly being obvious over Schreiber in view of Lin, Campbell, Green, and Owens. The rejection is respectfully traversed.

The Office is impermissibly using the application as a hindsight guide to reconstruct the claimed subject matter.[1] Schreiber does not disclose an antibody that selectively binds NIK protein comprising phosphorylated T559. Lin purportedly teaches that substitution of threonine at position 559 of SEQ ID NO: 5 abolishes NIK activity, and the Office asserted that it would have been obvious to one of ordinary skill to make an antibody that would bind to the NIK activation loop containing phosphorylated T559 to block NIK's activation site. However, modification of the Schreiber teaching to generate an antibody or antibody fragment that specifically binds NIK or a portion thereof comprising phosphorylated T559 was unpredictable prior to the instant invention. The Office asserted that "given that phosphorylated T559 was known in the art at the time of the invention was made, it would have been within the ordinary artisan's technical grasp to raise an antibody against a portion

of NIK that contains phosphorylated T559 and test the specificity of the antibody." Office Action, p. 12. This assertion ignores evidence provided in the specification that is directly contradictory to the Office's position. As explained above, the specification provides evidence that not all antibodies raised against the activation loop specifically bind the region of NIK comprising phosphorylated T559. In Example 1, polyclonal antibodies were generated using as immunogens three fragments of the NIK activation loop comprising amino acids 553-566, amino acids 553-562, or amino acids 549-560. All of the immunogenic fragments comprised phosphorylated T559. However, only the fragment comprising amino acids 549-560 (i.e., SEQ ID NO: 3, where the phosphorylated threonine residue was in the penultimate position) produced antibodies specific to phosphorylated NIK. Moreover, the specification discloses that a commercially available antibody claimed to be specific to T559-phosphorylated NIK did not work (i.e., did not specifically bind T559-phosphorylated NIK) and was removed from the vendor's catalogue. See p. 8, lines 3-7. Neither of the cited references provides a predictable basis for generating an anti-NIK antibody as currently claimed. Thus, there could not have been a reasonable expectation of success in generating anti-phospho-NIK antibodies, as asserted by the Office. The remaining secondary references, Campbell, Green and Owens, were cited as purportedly describing human, humanized, and chimeric antibodies or providing motivation for generating monoclonal antibodies, and fail to cure the deficiencies of Schreiber and Lin in rendering the invention obvious. Thus, the Office has not established a prima facie basis for rejecting the claims under § 103(a). Accordingly, the rejection of claims 1-10, 12, and 14-19 under 35 U.S.C. § 103(a) over Schreiber in view of Lin, Campbell, Green, and Owens, considered alone or in combination, has been overcome and should be withdrawn.

[1] Applicant is aware that, in a sense, all claim examinations must rely on hindsight. Applicant is asserting that, in this case, the hindsight used appears to have been impermissible in using the application as a guide to reconstructing the claims.

G. CONCLUSION

Applicants submit that the pending application is in condition for allowance. The Examiner is invited to contact the undersigned attorney by telephone if there are issues or questions concerning this submission that might be efficiently resolved in that manner.

Respectfully submitted,

Dated: February 17, 2011

By _____

Lance M. Shaner
Registration No.: 66,871
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive, Suite 6300
Willis Tower
Chicago, Illinois 60606-6357
(312) 474-6300
Attorney for Applicant